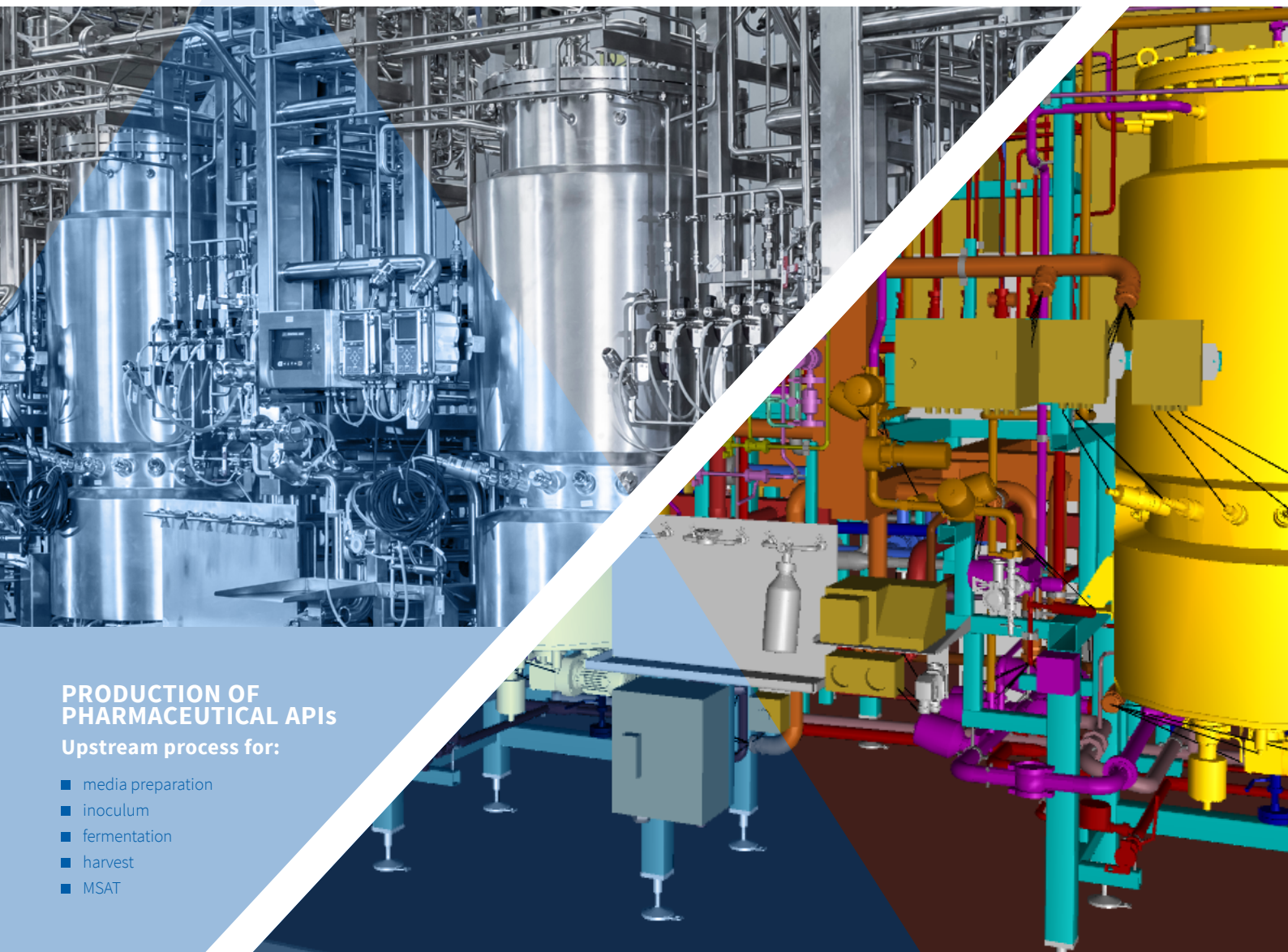


ZETA  
**BEST**  
PRACTICE



## PRODUCTION OF PHARMACEUTICAL APIs

Upstream process for:

- media preparation
- inoculum
- fermentation
- harvest
- MSAT

[www.zeta.com](http://www.zeta.com)

# A MAJOR PROJECT **MULTIPURPOSE PLANT FOR LARGE-SCALE CELL CULTURE**

Designed for the production of biopharmaceutical active ingredients for both the manufacturer's own products and contract manufacturing tasks for virtually every major pharmaceutical company worldwide.

## CHALLENGES

**A multipurpose plant has to be easily re-configured for product modifications** to cover a wide range of operating conditions. The plant design should cover a 100 production processes per year in one line.

**Rapid time-to-market as the key requirement** for the very tight project schedule has been reached based on tried and-tested technologies and thanks to ZETA's many years of experience in fast track project execution. An overall project completion time of a mere 36 months – starting from pre-basic engineering through to commissioning and the qualification on the customer premises – for such a ground-breaking project is altogether outstanding!

**The high complexity of project handling resulted from having no general contractor** who coordinated the multitude of PDPs. The responsibility for each interface and the coordination with PDPs had to be ensured individually. A new software-supported approach was used to close the coordination gap between the interface partners. The software has been implemented during the running project.

**To reduce both design complexity and 3D modelling efforts,** a specific "Master Copy Concept" was drawn up. A significant reduction of the time needed for detail engineering could be achieved by mirroring the plant design. The proven concept is also used for construction, commissioning and qualification.

**As the fabrication expert, ZETA took on the construction of highly complex utility piping.** The construction of the plant and the building at customer site have been executed at the same time, thus saving time.

**With MSAT a special technology unit has been developed to support the downscaling to pilot scale.** This equipment consists of 1x 20 L fermenter, 1x 80 L fermenter, 1x 150 L CIP station, 1x 130 L harvest and enables both development and launch of new products from a pipeline.



## A NEW DIMENSION IN AUSTRIAN BIOPHARMACEUTICAL MANUFACTURING

### TECHNICAL EXCELLENCE COUPLED WITH HIGH-QUALITY ENGINEERING

This remarkable project is part of a major 700 million euros investment to extend an existing research and biotech production plant in the heart of Europe.

ZETA engineering experts were entrusted with the pre-basic planning of the new facility that needs to cover the wide-ranging upstream process of a fermentation scale-up from 4 x 80 L to 6 x 12k L. Designing a state of the art multipurpose/ multiproduct with the flexibility to cover the future's need in terms of adaption for new products and process technologies, yet the stability, process safety and reproducibility have been the key requirements for plant engineering. Close cooperation in the multidisciplinary team of process, mechanical and automation engineers was mandatory for providing the pioneering innovations needed. A new processing approach in project planning kept this project on its tight schedule and made its execution in only 36 months possible.

#### Full Process Control enables

- monitoring and control of cell density and growth
- control of temperature, pH, stirrer speed and dissolved oxygen concentration
- ventilation by air and oxygen
- metabolites and CO<sub>2</sub> concentration monitoring
- process control by time-dependent addition of feed solutions and additives
- product formation monitoring

## CHALLENGES

### Super Skid Technology for free-hanging fermenters.

ZETA has developed a free-hanging super skid solution for up to 6,000 litre vessels for the best possible base cleaning capabilities. The special steel design had to be easy to integrate in the cleanroom. A temporary steel frame was installed during construction, which was then removed before relocating the system to the customer site. The advantage was clear: the fermenters were finished for full functional completeness and successfully passed the FAT.

### Industrial stirring with innovative magnetic mixing technology.

ZETA is the leading provider of magnetic mixing technology. With the magnetic agitator BMRF with a drive torque of over 700Nm for a bioreactor with a working volume of up to 15m<sup>3</sup>, the new technology for high scale mixing was able to demonstrate its benefits in a convincing manner. Sustainable improvements including minimization of contamination risks, thus avoiding subsequent product loss, are significant arguments for the implementation of the new technology.

### Inoculum incl. gas station for wave reactors.

A standard wave-reactor equipment had to be customized to establish a single-use inoculum train, fully compatible with customers' requirements in terms of automation and process safety. The single-use unit with tailor-made gassing station and automation is connected to the stainless steel environment.

### Qualification of all PDPs for this major project.

## RELEVANT KEY FIGURES

9 Wave Reactor systems  
**4x 80 L, 4x 400 L, 4x 2,000 L** seed fermenters  
**4x 2,000 L, 6 x 12k** production fermenters  
**3x 12k** fermenters (vessel only)  
**2x 2,500 L, 2x 6,000 L, 2x 15,000 L** media preparation  
**2x 18,000 L** harvest  
**1x 2,000 L** intermediate tank  
 CIP/SIP station for mobile vessels  
 Mobile vessels with docking stations  
 Inoculum incl. gas station for wave reactors  
 Filtertest station  
 MSAT  
**1 x 20 L** fermenter



### SCOPE OF SUPPLY

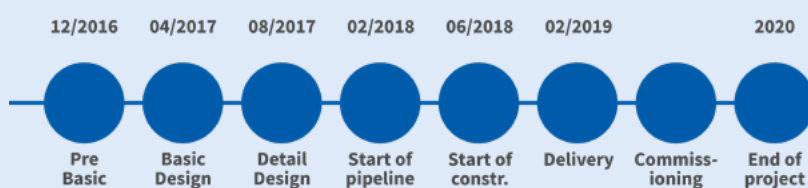
- Pre-basic engineering
- Basic engineering
- Detail engineering
- Cleanroom design
- Clean media
- Construction at ZETA Workshop
- FAT
- Site installation
- Commissioning
- Qualification

"This is a project of gigantic dimensions", Project Manager Martin Pichler puts it in a nutshell. Who, if not he should know. He continues: "I have been with ZETA for more than 15 years now and in this time have seen through numerous fast-track-projects for the company. Being part of such a major project is certainly not without high risks. But on the other hand it is always a welcome challenge and an opportunity for ZETA to display its expertise as a high-end engineer for pharmaceutical plant and a solution provider for both high value technology and perfect project management. An important success factor was definitely the exceptionally close and good cooperation between the customer and the high motivated ZETA Team!"



Free-hanging fermenters

## PROJECT EXECUTION TIME



# INNOVATIVE SOLUTIONS FOR OUR CUSTOMERS

## EVOLUTION OF TECHNOLOGY



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### ZETA Business Activities

Bioreactors & Fermentation Systems  
Downstream Systems  
Preparation Systems  
CIP/SIP Systems  
Magnetic Agitators  
Freeze & Thaw Systems  
Engineering  
Automation

### Customer Benefits

Deep process Understanding  
GMP FDA Compliance  
Super-Skid Design  
Focus on Sterility  
High process Reliability  
Scale-up Capabilities  
Experience in Complex Biologics  
Customized Process Systems

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